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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,432	11/23/1998	HOWARD A. FIELDS	03063-0231US	8029

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127 PEACHTREE STREET N E
ATLANTA, GA 30303-1811

EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

37

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/171,432

Applicant(s)

FIELDS ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69-82 is/are pending in the application.
- 4a) Of the above claim(s) 69,73-76 and 79-82 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 70-72,77 and 78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Status of the Claims

1. Claims 69-82 are currently pending in the present application. Claims 70-72, 77, and 78

~~are under consideration to the extent that they read on embodiments wherein the isolated,~~
antigenically reactive hepatitis A virus (HAV) peptide comprises a portion of the HAV P2A
protein, or conservative variations thereof. Claims 69, 73-76, and 79-82 have been withdrawn as
to non-elected inventions.

2. Claims 70-72, 77, and 78 were rejected in the prior Office Action, mailed on July 30,
2002 (the prior action). The Applicant amended claims 70, 71, 77, 79, and 81 in the Response
filed on January 8, 2003 (the Response)

3. The Art Unit location of your application, and the examiner to whom the case has been
docketed in the USPTO has changed. To aid in correlating any papers for this application, all
further correspondence regarding this application should be directed to Examiner Zachariah
Lucas in Art Unit 1648.

4. Because this action raises new grounds of rejection, not necessitated by amendments to
the claims, the action is being made Non-Final.

Specification

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5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the specification provides no antecedent basis for the claim language “specifically antigenically binds.”

Claim Objections

6. **(Prior Objection- Restated)** Claim 72 was objected to because of the following informalities: the word “the” was omitted from the last line of the claim. The Examiner disagrees with the Applicant’s traversal that the article “the” may alter the meaning of the claim. This is especially the case as the excluded sequences have already been introduced into the claims as “an amino acid sequence selected from the group consisting of SEQ ID NOS: 11-72.” However, if the Applicant does not wish to use the article “the,” it is suggested that the insertion of the article “an” between the “wherein” and the “amino acid sequence”, or the rearrangement of the claim such that it reads -- wherein at least one of the amino acid sequences selected from SEQ ID NOS: 38, and 42-46--, would not alter the meaning of the claim. In any case, some appropriate article introducing the amino acid sequences is required. Appropriate correction is required.

7. **(New Objection)** Claim 72 is objected to because of the following informalities: a comma would be appropriate to separate the claim elements of the reactive peptide and the excluded amino acid sequences. Appropriate correction is required.

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8. **(New Objection)** Claim 72 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim reads on the peptide of claim 70, wherein the peptide is selected from any of SEQ ID NOs: 11-72, and wherein at least one of SEQ ID NOs: 38-43 is excluded. For the purpose of this objection, the phrase “wherein amino acid sequence from at least one of SEQ ID NOS: 38-43 is excluded” is being interpreted as excluding any portion of the identified sequences.

This claim appears to read on any sequence of selected from SEQ ID NOs: 11-72, that specifically bind to an antibody reactive with SEQ ID NOs: 38, or 42-46. Because each of SEQ ID NOs: 38-43 include exclude at least a portion of one the other sequences of SEQ ID NOs: 38-43, the claim does not exclude any sequence as the antigenically reactive peptide. Thus, this claim is broader than claim 70 from which it depends, which requires the sequence to bind to an antibody specifically reactive with one SEQ ID NOs: 38, and 42-46. Thus, claim 70 excludes the (elected) sequences 39-41, which are reintroduced, and not excluded, in claim 72. For this reason, claim 72 is improperly dependant on claim 70.

9. **(Prior Objection- Maintained)** Claim 78 was objected to because of the following informalities: no article was provided between the words “of” and “sequence.” The applicant’s traversal is noted, but not found persuasive. Stating that that peptide contains no portion of “a” or “any” sequence, or “of one of more sequences” would not be inappropriate, or alter the meaning of the claim. Appropriate correction is therefore required.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. **(Prior Rejection- Withdrawn)** Claim 70 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The traversal was persuasive. The rejection is withdrawn.

12. **(Prior Rejection- Withdrawn)** Claim 70, and its dependant claims 71, 72, 77, and 78 rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicant traversed the rejection on two grounds. First that the art and the specification teach an HAV polyprotein, and therefore that it would have been clear to one in the art that the polyprotein was the source of the residue numeric identifiers used in the present claims, and that the Examiner used these numbers in a prior art rejection- and thus that the examiner clearly understood the claim.

First, it is noted that although the art and the specification refer to the HAV polyprotein, neither the specification, nor the claims, indicate that the numbers used to identify the HAV proteins are determined based on this sequence. Thus, the claim was indefinite as the amino acid

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sequence to which the applicant was referring is unclear. Second, the applicant argues that because the Examiner made rejections referring to these numbers, the Examiner is implicitly acknowledging the clarity of the claims. This is incorrect. Rather, any rejection by the Examiner was a representation of the Examiner's best guess at the meaning of the claim. The fact that the Examiner happened to be correct in this instance does not indicate that the claim is definite.

13. **(Prior Rejection-Withdrawn)** Claim 71 was rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim was rejected for indefiniteness because of the use of the descriptive "small" in relation to the percentage of amino acids subject to modification. The applicant's traversal was persuasive, and the rejection is therefore withdrawn.

14. **(New Rejection)** Claim 72 is rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on antigenically reactive HAV peptides selected from SEQ ID NOs: 11-72, "wherein amino acid sequence from at least one of SEQ ID NOS: 38-43 is excluded." The claim is indefinite because it is unclear from the claim whether the term "amino acid sequence" referred to in the quoted phrase excludes an entire amino acid sequence from one of the identified sequences, or if the phrase requires the exclusion of any sequence of the identified peptides (i.e. a portion of the sequence). It is suggested that the

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insertion of one of the suggested articles into the claim prior to the term “amino acid sequence” would clarify the claim’s meaning.

This claim is also indefinite because it is not clear from the claim what is meant by “an antibody specifically antigenically reactive” with the claims peptide. Claim 72 further identifies the peptide of claim 70, which binds an antibody specifically antigenically reactive with a peptide selected from the group consisting of SEQ ID NOs: 38, 42-46, and conservative variations thereof. Claim 72 further describes these peptides as any peptide selected from SEQ ID NOs: 11-72, wherein “wherein amino acid sequence from at least one of SEQ ID NOS: 38-43 is excluded.” It is unclear how an antibody that is specifically reactive with a peptide of SEQ ID NOs: 38, or 42-46 could be a peptide other than those according to SEQ ID NOs: 38, or 42-46. However, as the claim indicates that such is the case, it becomes unclear what is meant by “specifically reactive.” It is also unclear as to what is meant by the phrase “antigenically binds.” The applicant has provided definitions in the specification for the term “specifically immunoreactive with.” Because it is generally assumed that different terms in a claim mean different things, the use of the different language in the claims and the specification may be assumed to have different languages. It is therefore unclear what is meant by the identified claim language.

15. **(New Rejection)** Claim 78 is rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on antigenically reactive HAV peptides “wherein the peptide contains no portion of sequence selected from the group of SEQ

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ID NOS: 38-43.” The claim is indefinite because it is unclear from the claim whether the amino acid sequence referred to in the quoted phrase excludes any amino acid sequence from the identified sequences, or if the phrase excludes only portions of a single sequence selected from the identified group of sequences. The claim could be clarified by inserting either the phrase

-----“any” (if portions of all, or more than one, of the sequences are to be excluded) or “a” (if portions of only a single sequence is to be excluded at one time) in front of the word “sequence” in the quoted phrase.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. **(Prior Rejection-Withdrawn)** Claim 72 was rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The applicant's arguments were persuasive. The rejection is therefore withdrawn.

18. **(New Rejection)** Claims 70-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antigenically reactive peptide consisting of one of SEQ ID NO: 38, or 42-46, does not reasonably provide enablement for any portion of the HAV

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polyprotein comprising one of these sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. In the traversal of the 103 rejection over Chiron, the applicant pointed out that the prior art (Jia et al., J. Infect. Dis. 165:273-80) teaches that denaturation of full-length HAV-proteins leads to loss of binding of the proteins by anti-HAV antibodies. As the applicant points out, the art indicates that proteins or polypeptides that vary in conformation from the whole protein (un-denatured) are not antigenic.

In the present application, the applicant has shown that specific [peptides of approximately 18 to 20 residues are able to bind anti-HAV antibodies. Thus, the applicant is enabled for these peptides. However, the applicant has not shown that these peptides, or any polypeptide comprising them (i.e. any portion of an HAV protein comprising these peptides) would be capable of binding anti-HAV antibodies. Nor has the applicant demonstrated that residue conformation is not required for antibody binding as was described by Jia. Because the applicant has not indicated what combinations of peptides, or what portions of the proteins, are or are not able to bind anti-HAV PA2 antibodies, other than the identified sequences of SEQ ID NOs: 38-46, the applicant is not enabled for any portion of this protein that comprises one of these peptides. The applicant is enabled for only the whole PA2 protein, which is not being claimed (and has been described in Jia), and for the specifically identified peptides which have been shown to bind anti-HAV antibodies.

Further, with regards to claim 71, the claimed peptides would, according to the teachings of Jia, appear to conformational in nature. As conformational epitopes are unpredictable in nature, and as the applicant has not demonstrated any operable variations of the identified

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peptides, nor provided any guidance as to what substitutions of other alterations would, or would not have an effect on antibody binding to the peptides, the applicant is not enabled for variations to the identified peptides.

19. **(New Rejection)** Claims 70-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For the purposes of this rejection, claim 72 will be treated as representative of the rejected claims; and the phrase "wherein amino acid sequence from at least one of SEQ ID NOS: 38-43 is excluded" is being read as excluding at least a portion of one of SEQ ID NOS: 38-43. This claim reads on antigenically reactive peptides according to claim 70 wherein the peptide has an amino acid sequences selected from one of SEQ ID NOS: 11-72, and wherein the sequence of at least one of SEQ ID NOS: 38-43 are excluded. Because the claim depends from claim 70, the peptides must also react with an antibody that is specifically antigenically reactive with a peptide selected from SEQ ID NOS: 38, and 42-46.

As described above, claim 72 reads on any of SEQ ID NOS: 11-72, wherein said peptide binds with an antibody that specifically reacts with one of the peptides of SEQ ID NOS: 38, and 42-46. However, an antibody that specifically binds a peptide is indicated by the application (on page 12, lines 17-29) to require that the antibody preferentially bind a particular peptide, and not significantly bind other peptides, in a sample. In such a case, an antibody that specifically binds one of SEQ ID NOS: 38, or 42-46, would not be expected to specifically bind one of SEQ ID

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NOs: 11-72 other than one of SEQ ID NOs: 38, or 42-46. As the applicant has not disclosed either an antibody that would bind all of these peptides, or a motif or common characteristic that would indicate that all of the peptides of SEQ ID NOs: 11-72 would be bound by the antibodies of claim 70, the applicant has not provided sufficient written description to support the limitations of claim 72.

20. **(New Rejection)** Claim 72 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies antigenic peptides comprising SEQ ID NO: 38, or 42-46 that bind antibodies that specifically bind one of SEQ ID NOs: 38, or 42-46, does not reasonably provide enablement for any peptide according SEQ ID NOs: 11-72 that bind such an antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. This claim has been described above.

The applicant has also indicated what is meant by the phrase “specifically binds to.” As one skilled in the art would also assume that an antibody that specifically binds to a peptide would preferentially bind that peptide, and not to others, the applicants definition is accepted. However, the applicant is therefore claiming any peptide according to SEQ ID NOs: 11-72, that is capable of binding an antibody that specifically binds to one of SEQ ID NOs: 38, and 42-46. As an antibody that binds any one of SEQ ID NOs: 38, or 42-46 would not specifically bind any of the sequences of SEQ ID NOs: 11-72 other than the peptide of SEQ ID NO: 38, or 42-46, the applicant is not enabled for any of the sequences identified in claim 72 other than SEQ ID NOs: 38, and 42-46. Thus, the claims are not enabled to its full scope.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. **(Prior Rejection- Maintained)** In the prior action, claims 70-72, 77, and 78 were rejected as anticipated under 35 U.S.C. 102(b) by Robertson et al., Journal of General Virology 73:1365-1377. Robertson taught a number of peptides of the HAV polyprotein sequence. Among these peptides was the one identified by the Gen Core Accession number PQ0431. Amino residues 16-35 of this sequence are identical to the sequence of SEQ ID NO: 38. See also, Gencore Accession number PQ0427, which discloses the same sequence with a conservative substitution for the Lysine of position 788. Both sequences are disclosed in Figure 2 of the reference. Thus, although claims 70-72, 77, and 78 have been amended in an attempt to avoid the rejection, the rejection is maintained for the reasons indicated above.

23. **(New Rejection)** Claim 70 is rejected under 35 U.S.C. 102(b) as being anticipated by Jia et al., Journal of Infectious Diseases, 165:273-80 (1992- of record in the IDS filed on August 23, 2001). The claim reads on any antigenically reactive peptide comprising a portion of a HAV P2A protein. However, the specification does not define or set a limit on the size of the claimed

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peptides, or require that the peptides not comprise a complete HAV protein. Jia discloses a P2 protein of HAV that binds with anti-HAV antibodies isolated from the sera of infected subjects. Abstract. As this protein comprises the P2A protein, and as it therefore also comprises the sequences of SEQ ID NOs: 38-46, and therefore be able to bind antibodies specific thereto, the reference anticipates the claim.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25. **(Prior Rejection- Maintained)** Claims 70-72 were rejected in the prior action under 35 U.S.C. 103(a) as being obvious over Chiron Corp., EP 0199480. The applicant has traversed this rejection on the grounds that the Jia reference teaches away from the operability of the peptides taught by Chiron. The Examiner does not find the traversal persuasive. The Chiron reference teaches that there are epitopes within the HAV sequence of residues 792-848 of the HAV polypeptide. One of ordinary skill in the art would have been able to identify such peptides by screening such against animal sera. While Jia teaches that the denatured form of the protein, thus linear peptides, would not be operative, it does not teach that no peptides derived from the P2 protein would react with antibodies from an HAV infected subject.

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Chiron, also, does not state that the HAV epitopes are in linear form. It does, however, teach that there are epitopes, whether linear or conformational, in the identified sequence. As one of ordinary skill in the art would have been able to screen fragments of the sequence for reactivity against antibodies, the reference still renders to claims obvious, though it does not render the identified sequences obvious.

Conclusion

26. No claims are allowed.

27. Claims to the peptides of SEQ ID NOs: 42-46 would be allowable over the prior art.

28. It is noted that claims 79-81 read on combinations of the elected peptides (subcombinations) with (fused to) other peptides. Upon the determination that elected claims are allowable, claims to the allowable peptides in combination with other peptides will be rejoined if such claims incorporate all of the limitations of, and raise no new patentability issues to, the elected subject matter.

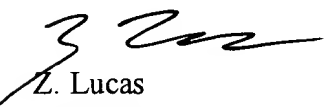
29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

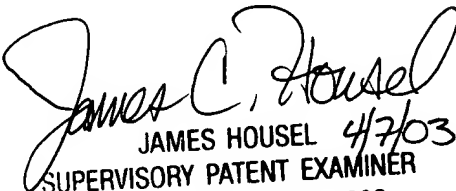
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

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organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
April 7, 2003


JAMES HOUSEL 4/7/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600